REMARKS

Reconsideration of the present application in view of the above amendments and the following remarks is respectfully requested. Claims 102-124 were pending. Claims 103, 104, 113 and 114 have been canceled without prejudice to future prosecution in a related application. Accordingly, claims 102, 105-112 and 115-124 are pending. Claim 102 has been amended to incorporate the features recited in previously pending claims 103, 113 and 114. Claim 124 has also been similarly amended. Claims 109, 110, 118, 119 and 121 have been amended to enter minor editorial changes in view of the amendments to claim 102. The above amendments have been made to facilitate allowance and without acquiescence to the rejections in the Office Action. No new matter has been added.

Interview Summary

Applicants' representative thanks the Examiner for the interview of January 12, 2006. Applicants' representative confirms that the Interview Summary attached to the Office Action is accurate.

Claim Rejections Under 35 U.S.C. § 102(b)

Claims 102-111, 113-115, 117, 118 and 122-124 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Dale *et al.* (U.S. Patent No. 5,856,092, referred to as "Dale" below). More specifically, it is asserted that every limitation recited in the rejected claims is disclosed in Dale.

Applicants respectfully traverse this ground of rejection. Applicants submit that Dale fails to disclose several features recited in claim 102. First, Dale fails to disclose a targeting element comprising an oligonucleotide that (i) binds specifically to a target genomic DNA sequence of a genomic DNA molecule of interest in a population of genomic DNA molecules, and (ii) overlaps a distinguishing element of the genomic DNA molecule of interest at or near the 3' end of the oligonucleotide as recited in step (b) of claim 102. The distinguishing

element recited in claim 102 distinguishes the genomic DNA molecule of interest from the other genomic DNA molecule of different haplotype (*see*, proviso (a)(3) of claim 102). Such a distinguishing element is not described in column 7, lines 8-17 of Dale, which is specifically cited in the Action as the description of step (b) of claim 102 in Dale. Nor does the remaining portion of Dale provide the description of step (b) of claim 102. More specifically, Dale relates to two types of detection methods: the detection of a specific polynucleotide sequence and the detection of a specific nucleotide at a particular position in a polynucleotide sequence. As to the former method, the detection depends on a sequence specific primer that distinguishes a polynucleotide sequence of interest and other unrelated sequences. Accordingly, in Dale, there is no mention of, or no need to mention, anything corresponding to the distinguishing element that distinguishes a genomic DNA molecule of interest from another genomic DNA molecule of different haplotype. As to the latter method, the detection depends on extension of a primer in the presence of at least one terminating ddNTP up to and including a specific nucleotide of interest (*see*, *e.g.*, claim 1 of Dale). Assuming that the specific nucleotide of interest in Dale corresponds to the distinguishing element of the present invention, because the resulting extension product in Dale would correspond to a targeting element with a separation group already attached to it, not to the targeting element itself, of the present application, Dale fails to disclose a targeting element that comprises an oligonucleotide that overlaps the distinguishing element at or near the 3'-end of the oligonucleotide.

Second, Dale fails to disclose the characterization of a genomic DNA molecule of interest after being separating from another genomic DNA molecule of different haplotype as recited in step (f) of claim 102. As discussed above, Dale relates to nucleic acid <u>detection</u> methods. Throughout this reference, it is emphasized that the novelty of the disclosed invention lies in the use of a single capture/detector system (*e.g.*, column 2, lines 2-4, 39, 40). The only molecules that contain both capture and detector elements disclosed in Dale are extension products made using a nucleic acid molecule whose presence in a biological sample is of interest as a template. For the above-noted novelty to be realized, Dale discloses the detection of the extension products to indicate the presence of the nucleic acid molecule of interest in the biological sample, not the direct characterization of the nucleic acid molecule of interest from the

biological sample. In this regard, Applicants respectfully disagree with the assertion in the Action regarding claim 113: "Dale et al disclose the method further comprising characterizing the molecule of interest (Example 2 and Fig. 2b)." Although the template DNA was annealed to the extension product when the extension product was analyzed in Example 2 and Fig. 2b (rather than the template DNA), only the extension product was characterized due to the presence of detector elements in the extension product (and the absence of detector elements in the template DNA).

Third, Dale fails to disclose the characterization of the sites in a genomic DNA molecule of interest that constitute a haplotype as recited in step (f) of claim 102. There is no mention of haploid-specific nucleic acid isolation in this reference. In addition, the disclosure related to single nucleotide polymorphism detection in Dale is insufficient to teach the haplotyping method of the present invention. One single nucleotide polymorphism (SNP) by itself does not constitute a haplotype, nor does a collection of SNPs alone. A haplotype is only generated by the linked association of SNP genotypes across a region of DNA. The specific sections cited in the Action in supporting the rejection against claim 114 (*i.e.*, Example 2; column 24, lines 45-47; and Fig. 2b) do not disclose haploid-specific nucleic acid isolation or characterization. Example 2 relates to the detection of single stranded genomic DNA from the bacteriophage M13 mp1 (which is a non-eukaryotic organism): There would be no need to consider the haploid separation of such a nucleic acid molecule of interest.

In view of the above remarks, Applicants submit that this ground of rejection under 35 U.S.C. § 102(b) has been overcome. Withdrawal of this rejection is respectfully requested.

Claim Rejections Under 35 U.S.C. § 103(a)

Claim 112 stands rejected under 35 U.S.C. 103(a) as allegedly unpatentable over Dale *et al.* (U.S. Patent. No. 5,856,092, "Dale") in view of Vary *et al.* (U.S. Patent No. 4,851,331, referred to as "Vary" below). More specifically, it is asserted in the Action that (1) Dale discloses every element recited in claim 111, (2) Vary teaches primers complementary to the sequence of interest at the 3' end of the primers, (3) it would have been obvious for one of

ordinary skill in the art to apply the 3' specific primers of Vary to the sequence-specific primer extension of Dale, and (4) such a person would have been motivated to do so for the expected benefit of extending and detecting only the sequence of interest as desired in the art.

Applicants respectfully traverse this ground of rejection. Applicants submit that the cited references, either alone or in combination as indicated in the Action, do not teach or suggest the subject matter as currently claimed in the present application. More specifically, as discussed above, Dale fails to disclose (1) a targeting element comprising an oligonucleotide that (i) binds specifically to a target genomic DNA sequence of a genomic DNA molecule of interest in a population of genomic DNA molecules, and (ii) overlaps a distinguishing element of the genomic DNA molecule of interest at or near the 3' end of the oligonucleotide as recited in step (b) of claim 102; (2) the characterization of a genomic DNA molecule of interest after being separated from another genomic DNA molecule of different haplotype as recited in step (f) of claim 102; and (3) the characterization of the sites in the genomic DNA molecule of interest that constitute a haplotype as recited in step (f) of claim 102.

Vary fails to remedy the last two deficiencies in Dale. More specifically, similar to Dale, Vary also relates to a nucleic acid detection method, not a haploid-specific isolation and characterization method of the present invention. Primer extension products, rather than nucleic acid molecules of interest from a biological sample, are characterized and detected in Vary. In addition, Vary also fails to teach or suggest the characterization of the sites in nucleic acid molecules of interest that constitute a haplotype as claimed in the present application.

Moreover, Applicants submit that no sufficient motivation is provided in the Action for one of ordinary skill in the art to combine Dale with Vary. More specifically, as discussed above, Dale relates to two types of detection methods: the detection of a specific polynucleotide sequence and the detection of a specific nucleotide at a particular position in a polynucleotide sequence. As to the former method, because a sequence specific primer in Dale would be sufficient to distinguish a polynucleotide sequence of interest and other unrelated sequences and to allow for the extension and detection of only the nucleic acid sequence of interest (which is the motivation provided in the Action for combining Dale with Vary), there would not have been any motivation for one of ordinary skill in the art to complicate the method

of Dale by combining with Vary. As to the latter method of Dale, the detection depends on extension of a primer in the presence of at least one terminating ddNTP up to and including a specific nucleotide of interest that distinguishes a nucleic acid molecule from another related nucleic acid molecule. Because Vary requires a primer to either form a match or mismatch with a nucleic acid molecule at the position of a specific nucleotide of interest, the combination of the latter method of Dale with Vary would make that method of Dale inoperable.

Claim 116 stands rejected under 35 U.S.C. 103(a) as allegedly unpatentable over Dale *et al.* (U.S. Patent No. 5,856,092, "Dale") in view of Zhou *et al.* (U.S. Patent No. 6,355,491, referred to as "Zhou" below).

Applicants respectfully traverse this ground of rejection. Applicants submit that the cited references, either alone or in combination as indicated in the Action, do not teach or suggest the subject matter as currently claimed in the present application. More specifically, Zhou relates to electromagnetic chips and electromagnetic biochips having arrays of individually addressable micro-electromagnetic units, as well as methods of utilizing these chips for directed manipulation of micro-particles and micro-structures such as biomolecules and chemical reagents. This reference fails to remedy the deficiencies of Dale in teaching or suggesting steps (b) and (f) recited in claim 102.

Claims 119 and 120 stand rejected under 35 U.S.C. 103(a) as allegedly unpatentable over Dale *et al.* (U.S. Patent No. 5,856,092, "Dale") in view of Radding *et al.* (U.S. Patent No. 4,888,274, referred to as "Radding" below).

Applicants respectfully traverse this ground of rejection. Applicants submit that the cited references, either alone or in combination as indicated in the Action, do not teach or suggest the subject matter as currently claimed in the present application. More specifically, Radding relates to a single-stranded nucleoprotein filament adapted to complex with a target duplex DNA having a selected base sequence. This reference fails to remedy the deficiencies of Dale in teaching or suggesting steps (b) and (f) recited in claim 102.

Claim 121 stands rejected under 35 U.S.C. 103(a) as allegedly unpatentable over Dale *et al.* (U.S. Patent No. 5,856,092) in view of Lebo (U.S. Patent No. 5,654,148, referred to as "Lebo" below).

Applicants respectfully traverse this ground of rejection. Applicants submit that the cited references, either alone or in combination as indicated in the Action, do not teach or suggest the subject matter as currently claimed in the present application. More specifically, Lebo relates to methods for analyzing prenatal cell samples by in situ hybridization. It fails to remedy the failure of Dale in teaching or suggesting step (b) recited in claim 102.

In view of the above remarks, Applicants submit that the aforementioned rejections under 35 U.S.C. 103(a) have been overcome. Withdrawal of these rejections is respectfully requested.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Applicants believe that all of the claims remaining in the application are now allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

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